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CLAIMS

We claim:

- 1. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) at least one erb family inhibitor and (ii) at least one Raf and/or ras inhibitor.
- 2. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a cRaf-1 inhibitor.
- 3. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (I)

or a salt, solvate, physiologically functional derivative thereof;

wherein

Y is CR¹ and V is N; or Y is CR¹ and V is CR²;

R¹ represents a group CH₃SO₂CH₂CH₂NHCH₂-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C₁₋₄ alkyl or C₁₋₄ alkoxy groups;

R² is selected from the group comprising hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino and di[C₁₋₄ alkyl]amino;

U represents a phenyl, pyridyl, $3\underline{H}$ -imidazolyl, indolyl, isoindolyl, indolyl, isoindolyl, $1\underline{H}$ -indazolyl, 2,3-dihydro- $1\underline{H}$ -indazolyl, $1\underline{H}$ -benzimidazolyl, 2,3-dihydro- $1\underline{H}$ -benzimidazolyl or $1\underline{H}$ -benzotriazolyl group, substituted by an R^3 group and optionally substituted by at least one independently selected R^4 group;

R³ is selected from a group comprising benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R3 represents trihalomethylbenzyl or trihalomethylbenzyloxy;

or R3 represents a group of formula

wherein each R^5 is independently selected from halogen, C_{1-4} alkyl and C_{1-4} alkoxy; and n is 0 to 3;

each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulphinyl, C₁₋₄ alkylsulphonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxycarbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro and trifluoromethyl; and

(ii) a cRaf-1 inhibitor.

4. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (II):

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$$H_3C \stackrel{Q}{\stackrel{N}{\circ}} \stackrel{H}{\stackrel{\sim}{\circ}} \stackrel{Z}{\stackrel{\sim}{\circ}} \stackrel{N}{\stackrel{\sim}{\circ}} \stackrel{N}{\stackrel{\sim}{\circ}} \stackrel{N}{\stackrel{\sim}{\circ}} \stackrel{(II)}{\stackrel{\sim}{\circ}}$$

and salt or solvates thereof, wherein R is -Cl or -Br, X is CH, N, or CF, and Z is thiazole or furan; and

(ii) a cRaf-1 inhibitor.

5. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (III):

and salts or solvates thereof; and

(ii) a cRaf-1 inhibitor.

- 6. A cancer treatment combination, comprising: therapeutically effective amounts of (i) at least one erb family inhibitor and (ii) at least one Raf and/or ras inhibitor.
- 7. A cancer treatment combination, comprising: therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a cRaf-1 inhibitor.

8. A cancer treatment combination, comprising: therapeutically effective amounts of (i) a compound of formula (I)

or a salt, solvate, or physiologically functional derivative thereof;

wherein

Y is CR¹ and V is N; or Y is CR¹ and V is CR²;

R¹ represents a group CH₃SO₂CH₂CH₂NHCH₂-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C₁₋₄ alkyl or C₁₋₄ alkoxy groups;

R² is selected from the group comprising hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino and di[C₁₋₄ alkyl]amino;

U represents a phenyl, pyridyl, $3\underline{H}$ -imidazolyl, indolyl, isoindolyl, isoindolyl, isoindolyl, $1\underline{H}$ -indazolyl, 2,3-dihydro- $1\underline{H}$ -indazolyl, $1\underline{H}$ -benzimidazolyl, 2,3-dihydro- $1\underline{H}$ -benzimidazolyl or $1\underline{H}$ -benzotriazolyl group, substituted by an R^3 group and optionally substituted by at least one independently selected R^4 group;

R³ is selected from a group comprising benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R3 represents trihalomethylbenzyl or trihalomethylbenzyloxy;

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or R3 represents a group of formula

wherein each R5 is independently selected from halogen, C1-4 alkyl and C1-4 alkoxy; and n is 0 to 3;

each R4 is independently hydroxy, halogen, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, C1-4 alkoxy, amino, C1-4 alkylamino, di[C1-4 alkyl]amino, C1-4 alkylthio, C1-4 alkylsulphinyl, C1-4 alkylsulphonyl, C1-4 alkylcarbonyl, carboxy, carbamoyl, C1-4 alkoxycarbonyl, C1-4 alkanoylamino, N-(C1-4 alkyl)carbamoyl, N,N-di(C1-4 alkyl)carbamoyl, cyano, nitro and trifluoromethyl; and

(ii) a cRaf-1 inhibitor.

A cancer treatment combination, comprising: therapeutically effective 9. amounts of (i) a compound of formula (II):

and salt or solvates thereof, wherein R is -Cl or -Br, X is CH, N, or CF, and Z is thiazole or furan; and

(ii) a cRaf-1 inhibitor.

A cancer treatment combination, comprising: therapeutically effective 10. amounts of (i) a compound of formula (III):

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and salts or solvates thereof; and

(ii) a cRaf-1 inhibitor.

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11. A cancer treatment combination, comprising: therapeutically effective amounts of (i) at least one erb family inhibitor and (ii) at least one Raf and/or ras inhibitor for use in therapy.

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- 12. A cancer treatment combination, comprising: therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a cRaf-1 inhibitor for use in therapy.
- 13. Use of a cancer treatment combination, comprising: therapeutically effective amounts of (i) at least one erb family inhibitor and (ii) at least one Raf and/or ras inhibitor in the preparation of a medicament for use in the treatment of a susceptible cancer.
- 14. A cancer treatment combination, comprising: theraper-tically effective amounts of (i) an EGFR/erbB-2 inhibitor and (ii) a cRaf-1 inhibitor useful in the preparation of a medicament for use in the treatment of a susceptible cancer.
- 15. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a bRaf inhibitor.

16. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (I)

$$\bigvee_{\text{HN}} \bigvee_{\text{N}} \bigvee_{\text{H}} \qquad \text{(i)}$$

or a salt, solvate, physiologically functional derivative thereof;

wherein

Y is CR¹ and V is N; or Y is CR¹ and V is CR²;

R¹ represents a group CH₃SO₂CH₂CH₂NHCH₂-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C₁₋₄ alkyl or C₁₋₄ alkoxy groups;

R² is selected from the group comprising hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino and di[C₁₋₄ alkyl]amino;

U represents a phenyl, pyridyl, $3\underline{H}$ -imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, $1\underline{H}$ -indazolyl, 2,3-dihydro- $1\underline{H}$ -indazolyl, $1\underline{H}$ -benzimidazolyl, 2,3-dihydro- $1\underline{H}$ -benzimidazolyl or $1\underline{H}$ -benzotriazolyl group, substituted by an R^3 group and optionally substituted by at least one independently selected R^4 group;

R³ is selected from a group comprising benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R3 represents trihalomethylbenzyl or trihalomethylbenzyloxy;

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or R3 represents a group of formula

wherein each R^5 is independently selected from halogen, C_{1-4} alkyl and C_{1-4} alkoxy; and n is 0 to 3;

each R^4 is independently hydroxy, halogen, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di[C_{1-4} alkyl]amino, C_{1-4} alkylthio, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, C_{1-4} alkylcarbonyl, carboxy, carbamoyl, C_{1-4} alkoxycarbonyl, C_{1-4} alkyl)carbamoyl, C_{1-4} alkyl)carbamoyl, cyano, nitro and trifluoromethyl; and

(ii) a bRaf inhibitor.

17. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (II):

and salt or solvates thereof, wherein R is -Cl or -Br, X is CH , N, or CF, and Z is thiazole or furan; and

(ii) a bRaf inhibitor.

18. A method of treating a susceptible cancer in a mammal, comprising: administering to said mammal therapeutically effective amounts of (i) a compound of formula (III):

and salts or solvates thereof; and

- (ii) a bRaf inhibitor.
- 19. A cancer treatment combination, comprising: therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a bRaf inhibitor.
- 20. A cancer treatment combination, comprising: therapeutically effective amounts of (i) a compound of formula (I)

$$\bigvee_{\text{HN}} \bigvee_{\text{N}} \bigvee_{\text{H}} \qquad \text{(I)}$$

or a salt, solvate, or physiologically functional derivative thereof;

wherein

Y is CR1 and V is N:

or Y is CR1 and V is CR2;

R¹ represents a group CH₃SO₂CH₂CH₂NHCH₂-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C₁₋₄ alkyl or C₁₋₄ alkoxy groups;

 R^2 is selected from the group comprising hydrogen, halo, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino and di[C_{1-4} alkyl]amino;

U represents a phenyl, pyridyl, $3\underline{H}$ -imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, $1\underline{H}$ -indazolyl, 2,3-dihydro- $1\underline{H}$ -indazolyl, $1\underline{H}$ -benzimidazolyl, 2,3-dihydro- $1\underline{H}$ -benzimidazolyl or $1\underline{H}$ -benzotriazolyl group, substituted by an R^3 group and optionally substituted by at least one independently selected R^4 group;

R³ is selected from a group comprising benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R³ represents trihalomethylbenzyl or trihalomethylbenzyloxy;

or R3 represents a group of formula

$$-N = (R^5)_n$$

wherein each R^5 is independently selected from halogen, C_{1-4} alkyl and C_{1-4} alkoxy; and n is 0 to 3;

each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulphinyl, C₁₋₄ alkylsulphonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxycarbonyl, C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro and trifluoromethyl; and

(ii) a bRaf inhibitor.

21. A cancer treatment combination, comprising: therapeutically effective amounts of (i) a compound of formula (II):

and salt or solvates thereof, wherein R is -Cl or -Br, X is CH , N, or CF, and Z is thiazole or furan; and

(ii) a bRaf-1 inhibitor.

22. A cancer treatment combination, comprising: therapeutically effective amounts of (i) a compound of formula (III):

and salts or solvates thereof; and

(ii) a bRaf inhibitor.

23. A cancer treatment combination, comprising: therapeutically effective amounts of (i) an erbB-2 inhibitor and (ii) a bRaf inhibitor for use in therapy.

24. Use of a cancer treatment combination, comprising: therapeutically effective amounts of (i) an EGFR/erbB-2 inhibitor and (ii) a bRaf inhibitor in the preparation of a medicament for use in the treatment of a susceptible cancer.